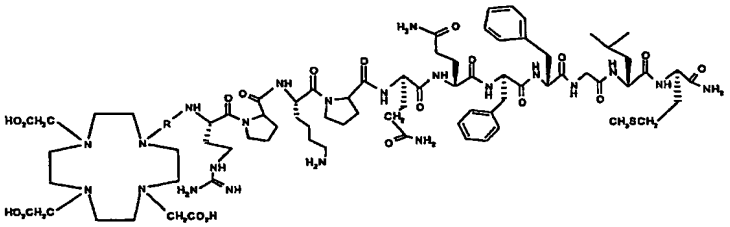
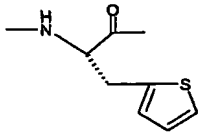
Claims:

1. Use of radio-nuclide labelled conjugates of substance P and a chelator molecule, having the abbreviation
Chelator-R-Arg^1-Pro^2-Lys^3-Pro^4-Gln^5-Gln^6-Phe^7-Phe^8-Gly^9-Leu^{10}-Met^{11}-NH_2 and comprising compounds of formula I

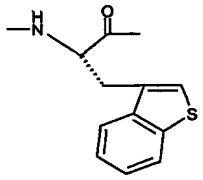


(I),

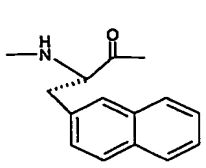
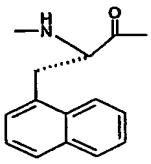
wherein
R is -CH_2-C(O)-, -C(CO_2H)CH_2CH_2-C(O)- or -C(CO_2H)CH_2-C(O)-,
or an analogue of formula I with at least one of the subsequent modifications in the amino acid sequence of substance P:
a) replacement of Met^{11} by -NH-CH(CH_2CH_2-SO_2-CH_3)-C(O)- (Met(O_2)^{11}), -NH-CH(CH_2CH_2-SO-CH_3)-C(O)- (Met(O)^{11}), or -NH-CH[CH(CH_3)CH_2CH_3)-C(O)- (Ile^{11}),
b) replacement of Leu^{10} by -NH-CH[CH(CH_3)CH_2CH_3)-C(O)- (Ile^{10}),
c) replacement of Gly^9 by -N(CH_3)-CH_2-C(O)- (Sar^9),
d) replacement of Phe^7 or Phe^8 or both Phe^7 and Phe^8 by residue of formulae

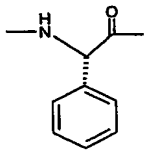
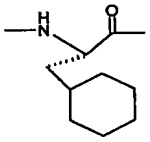


(2-Thi^{7,8}),

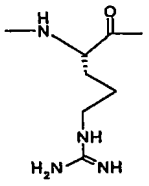
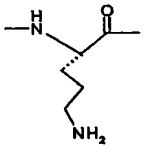


(3-BzThi^{7,8}),


(2-Nal^{7,8}),

(1-Nal^{7,8}),


(Phegly^{7,8}),

(Cha^{7,8}),

e) replacement of Lys^3 by residue of formulae


(Arg^3), or

(Orn^3),

f) truncation of 1 to 5 amino acids of the sequence Arg^1- Pro^2-Lys^3-Pro^4-Gln^5, or
g) replacement of 1 to 5 amino acids of the sequence Arg^1- Pro^2-Lys^3-Pro^4-Gln^5 by -N(CH_3)-CH_2-C(O)- (Sar),
and wherein the conjugate is labelled with a radio-nuclide selected from the group consisting of Actinium-225, Bismut-212, Bismut-213, Lead-203, Copper-64, Copper-67, Gallium-66, Gallium-67, Gallium-68, Lutetium-177, Indium-111, Indium-113, Yttrium-86 and Yttrium-90, Dyprosium162, Dysprosium 165, Dysprosium 167, Holmium-166, Praseodymium-142, Praseodymium-143, Promethium-149, and Terbium-149,
as active ingredient in radiopharmaceutical or radio-diagnostic formulations for targeting or treating brain tumors, especially gliomas.

2. Use according to claim 1, wherein the amino acid sequence in formula I corresponds to formulae

a) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met-NH_2,

b) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met(O_2)-NH_2,

c) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Sar-Leu-Met-NH_2,

d) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Gly-Leu-Met-NH_2,

e) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Phe-Gly-Leu-Met-NH_2,

f) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Sar-Leu-Met(O_2)-NH_2,

g) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Gly-Leu-Met(O_2)-NH_2,

h) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Phe-Gly-Leu-Met(O_2)-NH_2,

i) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Sar-Leu-Met(O_2)-NH_2,

j) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Phe-Sar-Leu-Met-NH_2,

k) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Phe-Sar-Leu-Met(O_2)-NH_2

l) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Thi-Sar-Leu-Met-NH_2,

m) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Thi-Sar-Leu-Met(O_2)-NH_2,

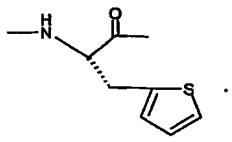
n) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Thi-Gly-Leu-Met-NH_2,

o) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Thi-Gly-Leu-Met(O_2)-NH_2.

3. Use according to claim 1, wherein the compounds of formula I comprise in the 11-position of the natural substance P sequence a methioninsulfone residue of formula -NH-$CH(CH_2CH_2$-SO_2-$CH_3)$-C(O)- instead of a methionin residue.

4. Use according to claim 1, wherein the glycin residue in position 9 of the natural substance P sequence is replaced by a sarcosin residue of formula -$N(CH_3)$-CH_2-C(O)-.

5. Use according to claim 1, wherein the phenylalanine residue in the 7- or 8-position or in both said positions of the natural substance P sequence is replaced by a 3-(2-thienyl)-alanine residue of formula



6. Use according to claim 1, wherein the phenylalanine residue in the 8-position of the natural substance P sequence is replaced by a 3-(2-thienyl)-alanine and the glycin residue in position 9 is replaced by a sarcosine residue.

7. Use according to claim 1, wherein the methionin residue in the 11-position of the natural substance P sequence is replaced by a methioninsulfone residue, and the phenylalanine residue in the 8-position of the natural substance P sequence is replaced by a 3-(2-thienyl)-alanine residue, or the glycin residue in position 9 is replaced by a sarcosine residue.

8. Use according to claim 1, wherein the amino acid sequence in formula I corresponds to formulae

a) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Gly-Leu-Met(O_2)-NH_2,

b) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Sar-Leu-Met-NH_2,

c) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Gly-Leu-Met-NH_2,

d) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Phe-Gly-Leu-Met-NH_2,

e) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Sar-Leu-Met(O_2)-NH_2,

f) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Gly-Leu-Met(O_2)-NH_2,

g) Arg-Pro-Lys-Pro-Gln-Gln-Thi-Thi-Gly-Leu-Met-NH_2, or

h) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Sar-Leu-Met(O_2)-NH_2.

9. Use according to claim 1, wherein the amino acid sequence in formula I corresponds to formulae

a) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Phe-Sar-Leu-Met(O_2)-NH_2, or

b) Arg-Pro-Lys-Pro-Gln-Gln-Phe-Thi-Gly-Leu-Met(O_2)-NH_2.

10. A method of targeting brain tumors, localizing or treating brain tumors and the satellite lesions thereof in a host afflicted with brain tumors, e.g. gliomas, in administrating to the host at least one compound of formula I or an analogue of a compound of formula I.

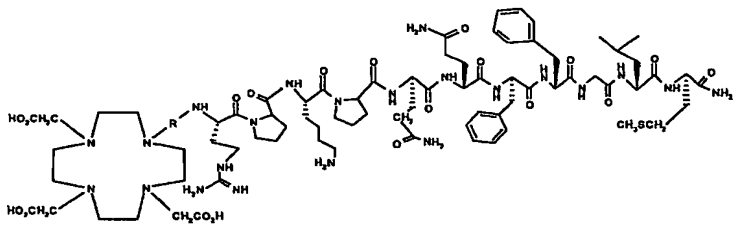
11. A therapeutic or diagnostic method for targeting brain tumors, localizing or treating brain tumors and the satellite lesions thereof in a mammal comprising administering to a mammal in need of such therapy, an effective amount of a radio-nuclide labelled substance P conjugate of formula I or an analogue thereof.

12. A method of delivering a radio-nuclide labelled substance P conjugate of formula I or an analogue thereof to a host, comprising administering to a host a radio-nuclide labelled substance P conjugate of formula I or an analogue thereof.

13. Use of a radio-nuclide labelled substance P conjugate of formula I or an analogue thereof for the manufacture of a medicament useful for the detection and therapeutic treatment of brain tumors and satellite lesions thereof in an mammal, such as a human.

14. A radio-nuclide labelled substance P conjugate of formula I or an analogue thereof for use in medical therapy.

15. Conjugates of substance P analogues and a chelator molecule, whereby substance P conjugate has the abbreviation
Chelator-R-Arg^1- Pro^2-Lys^3-Pro^4-Gln^5-Gln^6-Phe^7-Phe^8-Gly^9-Leu^{10}-Met^{11}-NH_2 and comprises compounds of formula I



(I),

wherein
R is $-CH_2-C(O)-$, $-C(CO_2H)CH_2CH_2-C(O)-$ or $-C(CO_2H)CH_2-C(O)-$, with the proviso that R is $-CH_2-C(O)-$, when the conjugate comprises the substance P sequence,

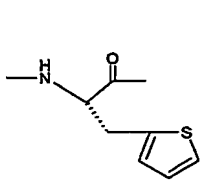
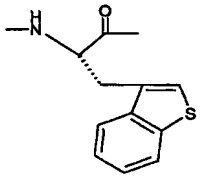
and an analogue of formula I with at least one of the subsequent modifications in the amino acid sequence of substance P:

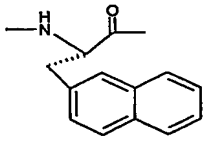
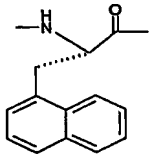
a) replacement of Met^{11} by -NH-CH(CH_2CH_2-SO_2-CH_3)-C(O)- ($Met(O_2)^{11}$), -NH-CH(CH_2CH_2-SO-CH_3)-C(O)- ($Met(O)^{11}$), or -NH-CH[CH(CH_3)CH_2CH_3]-C(O)- (Ile^{11}),

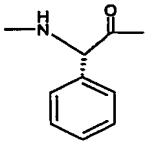
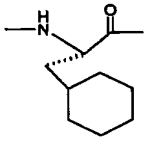
b) replacement of Leu^{10} by -NH-CH[CH(CH_3)CH_2CH_3]-C(O)- (Ile^{10}),

c) replacement of Gly^9 by -N(CH_3)-CH_2-C(O)- (Sar^9),

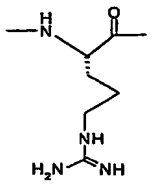
d) replacement of Phe^7 or Phe^8 or both Phe^7 and Phe^8 by residue of formulae


($2\text{-}Thi^{7,8}$),

($3\text{-}BzThi^{7,8}$),

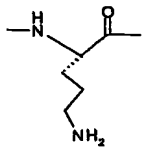

($2\text{-}Nal^{7,8}$),

($1\text{-}Nal^{7,8}$),


($Phegly^{7,8}$),

($Cha^{7,8}$),

e) replacement of Lys^3 by residue of formulae



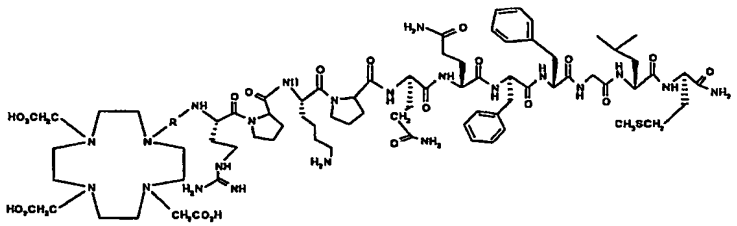
(Arg^3), or



(Orn^3),

f) truncation of 1 to 5 amino acids of the sequence Arg^1- Pro^2-Lys^3-Pro^4-Gln^5, or
g) replacement of 1 to 5 amino acids of the sequence Arg^1- Pro^2-Lys^3-Pro^4-Gln^5 by -$N(CH_3)$-CH_2-C(O)- (Sar),
and wherein the conjugates are unlabelled or labelled with a radio-nuclide selected from the group consisting of Actinium-225, Bismut-212, Bismut-213, Lead-203, Copper-64, Copper-67, Gallium-66, Gallium-67, Gallium-68, Lutetium-177, Indium-111, Indium-113, Yttrium-86 and Yttrium-90, Dyprosium162, Dysprosium 165, Dysprosium 167, Holmium-166, Praseodymium-142, Praseodymium-143, Promethium-149, and Terbium-149.

16. A composition comprising (a) at least one pharmaceutical carrier and (b) at least one conjugate of substance P or an analogue of substance P and a chelator molecule, whereby substance P conjugate has the abbreviation
Chelator-R-Arg^1- Pro^2-Lys^3-Pro^4-Gln^5-Gln^6-Phe^7-Phe^8-Gly^9-Leu^{10}-Met^{11}-NH_2 and comprises compounds of formula I



(I),

wherein

R is $-CH_2-C(O)-$, $-C(CO_2H)CH_2CH_2-C(O)-$ or $-C(CO_2H)CH_2-C(O)-$, with the proviso that R is $-CH_2-C(O)-$, when the conjugate comprises the substance P sequence,

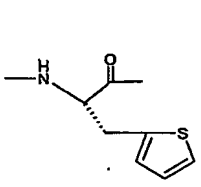
and an analogue of formula I with at least one of the subsequent modifications in the amino acid sequence of substance P:

a) replacement of Met^{11} by $-NH-CH(CH_2CH_2-SO_2-CH_3)-C(O)-$ ($Met(O_2)^{11}$), $-NH-CH(CH_2CH_2-SO-CH_3)-C(O)-$ ($Met(O)^{11}$), or $-NH-CH[CH(CH_3)CH_2CH_3)-C(O)-$ (Ile^{11}),

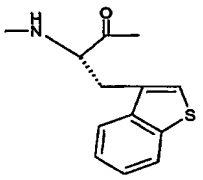
b) replacement of Leu^{10} by $-NH-CH[CH(CH_3)CH_2CH_3)-C(O)-$ (Ile^{10}),

c) replacement of Gly^9 by $-N(CH_3)-CH_2-C(O)-$ (Sar^9),

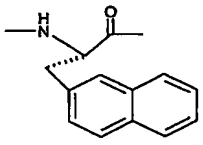
d) replacement of Phe^7 or Phe^8 or both Phe^7 and Phe^8 by residue of formulae



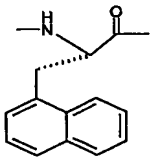
($2\text{-}Thi^{7,8}$),



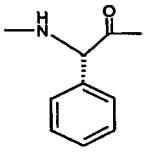
($3\text{-}BzThi^{7,8}$),



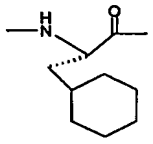
($2\text{-}Nal^{7,8}$),



($1\text{-}Nal^{7,8}$),

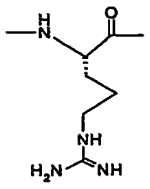


($Phegly^{7,8}$),

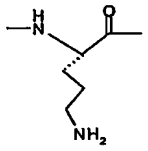


($Cha^{7,8}$),

e) replacement of Lys^3 by residue of formulae



(Arg^3), or



(Orn^3),

f) truncation of 1 to 5 amino acids of the sequence Arg^1-Pro^2-Lys^3-Pro^4-Gln^5, or
g) replacement of 1 to 5 amino acids of the sequence Arg^1-Pro^2-Lys^3-Pro^4-Gln^5 by -$N(CH_3)$-CH_2-C(O)- (Sar),
and wherein the conjugates are labelled with a radio-nuclide selected from the group consisting of Actinium-225, Bismut-212, Bismut-213, Lead-203, Copper-64, Copper-67, Gallium-66, Gallium-67, Gallium-68, Lutetium-177, Indium-111, Indium-113, Yttrium-86 and Yttrium-90, Dyprosium162, Dysprosium 165, Dysprosium 167, Holmium-166, Praseodymium-142, Praseodymium-143, Promethium-149, and Terbium-149.